

ACTIVITY OF CEFTAROLINE AND CEFTOBIPROLE AGAINST STAPHYLOCOCCI AND STREPTOCOCCUS PNEUMONIAE IN THE UK AND IRELAND

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INTRODUCTION

- Ceftaroline (Pfizer)¹ and ceftobiprole (Correvio)² are cephalosporins active against Gram-positive bacteria, including MRSA. Indications and clinical breakpoints differ (Table 1).
- There are few direct comparisons of their activity published.
- We reviewed comparative data for both agents vs.
 - staphylococci and pneumococci causing clinically-significant bacteraemia
 - pneumococci causing community-acquired pneumonia (CAP)

	Ceftaroline		Ceftobiprole	
Licensed Indications (UK/EU)	Acute skin and skin structure infections. CAP		CAP Hospital-acquired pneumonia (excl. ventilator-associated)	
Breakpoint	S	R	S	R
<i>S. aureus</i>	≤1mg/L	>2mg/L	≤2mg/L	>2mg/L
<i>S. pneumoniae</i>	≤0.25mg/L	>0.25mg/L	≤0.5mg/L	>0.5mg/L

TABLE 1. Licensed indications and EUCAST breakpoints⁶ for ceftaroline and ceftobiprole.

METHODS

- The BSAC Resistance Surveillance Programme³ has collected *S. aureus*, CoNS (coagulase-negative staphylococci) and *S. pneumoniae* causing clinically-significant bacteraemia between 2001 and 2017, and respiratory *S. pneumoniae* since 1999, from 22-39 hospitals throughout the UK and Ireland.
- Ceftaroline and ceftobiprole were tested in parallel by agar dilution⁴ in 2008, 2013 and 2017 for bloodstream isolates (all species) and in 2016/17 for respiratory *S. pneumoniae* only.
- CoNS were identified to species level in 2013 and 2017 by MALDI-ToF, but not in 2008.
- mecA* was sought by PCR.⁵
- Current EUCAST *S. aureus* breakpoints were assumed for CoNS (Table 1).

TO REQUEST ISOLATES

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RESULTS

- 3029 isolates were tested with both agents in the 3 non-consecutive years (Table 2).
- Modal and geometric mean MICs did not change significantly between years, except for CoNS tested with ceftobiprole where MICs rose for MR-CoNS and fell for MS-CoNS (Table 2).
- The geometric mean MICs of ceftobiprole varied by MR-CoNS species:
 - MR-*S. epidermidis* (215/291: 0.77)
 - MR-*S. haemolyticus* (33/36: 1.31)
 - MR-CoNS (other species) (53/105: 0.98)
- Rates of non-susceptibility to ceftaroline and ceftobiprole were low (Figure 1):
 - 10 (5%) MRSA and 42 (10%) MR-CoNS were non-susceptible to ceftaroline.
 - All *S. aureus* were susceptible to ceftobiprole.
 - 26/40 MR-CoNS were identified with ceftobiprole MIC >2mg/L; 22 (85%) were MR-*S. haemolyticus*.
 - 1 *S. pneumoniae* (serotype 19F) was non-susceptible to both ceftaroline and ceftobiprole.
 - 2 further *S. pneumoniae* (serotypes 19F and 19A) were non-susceptible to ceftobiprole only.

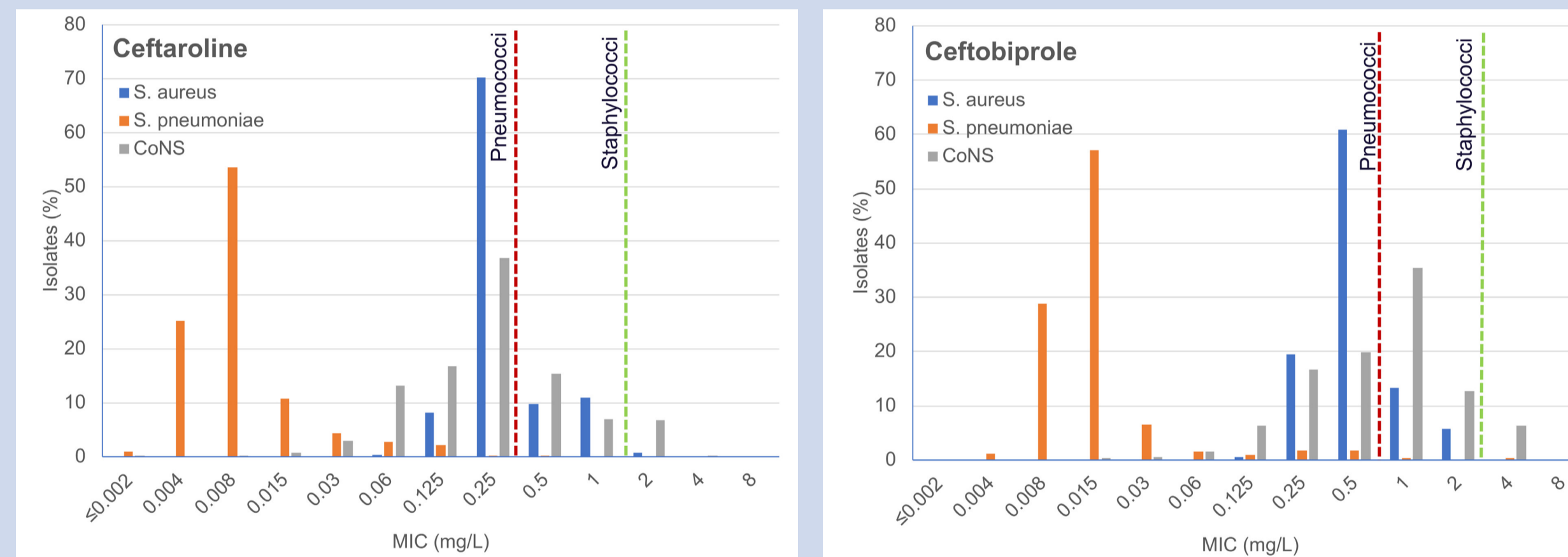


FIGURE 1. MIC distributions among staphylococci and pneumococci tested against ceftaroline and ceftobiprole. Dashed lines indicate EUCAST breakpoints.

	Total (n)	Ceftaroline MIC (mg/L)						Ceftobiprole MIC (mg/L)					
		2008	2013	2017	2008	2013	2017						
<i>S. aureus</i>	1428	Mode	Geo. mean	Mode	Geo. mean	Mode	Geo. mean	Mode	Geo. mean	Mode	Geo. mean	Mode	Geo. mean
MRSA	210	1	0.4	0.5	0.25	0.5	0.27	2	0.7	1	0.4	1	0.52
MSSA	1218	0.25	0.4	0.25	0.25	0.25	0.27	0.5	0.7	0.5	0.4	0.5	0.51
CoNS	612	0.25	0.24	0.25	0.22	0.25	0.23	1	0.67	0.5	0.64	0.25	0.66
MR-CoNS	431	0.25	0.24	0.25	0.28	0.25	0.35	1	0.67	0.5-1	0.8	1	1.03
MS-CoNS	181	0.06	0.24	0.06	0.14	0.06	0.1	0.25	0.69	0.25	0.41	0.25	0.27
<i>S. pneumoniae</i>	989	0.008	0.01	0.004	0.01	0.008	0.01	0.015	0.02	0.008	0.01	0.015	0.02

TABLE 2. Modal and geometric mean MICs of ceftaroline and ceftobiprole against staphylococci and pneumococci. MR: methicillin-resistant; MS: methicillin-susceptible. **Bold text:** change in modal MIC or geometric mean.

CONCLUSIONS

- Ceftaroline and ceftobiprole have similarly good activity against both staphylococci and pneumococci.
- Modal ceftaroline MICs for staphylococci tended to be c. 2-fold lower than ceftobiprole, but ceftobiprole has a 2-fold higher breakpoint.
- There were no changes in susceptibility of ceftaroline and ceftobiprole among *S. aureus* and pneumococci across the 10 years (2008-17).
- Changes in ceftobiprole MICs in CoNS were not due to changes in species distribution.
- Ceftobiprole MICs for MR-*S. haemolyticus* were >2mg/L in 22/33 (67%) cases compared with 2/215 (0.9%) MR-*S. epidermidis*.
- Ceftaroline MICs were also raised for MR-*S. haemolyticus* at 2mg/L.
- Choices regarding which agent to prefer should be predicated on other differentiating factors, e.g. licensed indications, reported clinical experience, and breadth of Gram-negative coverage.
- Continued collection of surveillance data is crucial for our understanding of antibiotic resistance trends in the UK and Ireland.

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